

residues, such as about 300 amino acid residues, for example less than 300 amino acid residues, such as about 290 amino acid residues, for example 290 amino acid residues.

A fragment comprising the Hp-Hb binding region of native CD163 is particularly preferred. However, the invention is not limited to fragments comprising the Hp-Hb binding region. Deletions of such fragments generating functionally equivalent fragments of CD163 comprising less than the Hp-Hb binding region are also comprised in the present invention. Functionally equivalent CD163 peptides, and fragments thereof according to the present invention, may comprise less or more amino acid residues than the Hp-Hb binding region.

Fragments comprising the Hp-Hb binding region preferably comprises the SRCR domains I-IX of the CD163 receptor, such as capable of binding to a region in the SRCR domains I-VIII of the CD163 receptor, capable of binding to a region in the SRCR domains I-VII of the CD163 receptor, capable of binding to a region in the SRCR domains I-VI of the CD163 receptor, capable of binding to a region in the SRCR domains I-V of the CD163 receptor, capable of binding to a region in the SRCR domains I-IV of the CD163 receptor, capable of binding to a region in the SRCR domains I-III of the CD163 receptor, capable of binding to a region in the SRCR domains I-II of the CD163 receptor, or a variant thereof.

In a preferred embodiment the fragments comprising the Hp-Hb binding region preferably comprises the SRCR domains I-IX of the CD163 receptor, such as capable of binding to a region in the SRCR domains III-IX of the CD163 receptor, capable of binding to a region in the SRCR domains III-VIII of the CD163 receptor, capable of binding to a region in the SRCR domains III-VII of the CD163 receptor, capable of binding to a region in the SRCR domains III-VI of the CD163 receptor, capable of binding to a region in the SRCR domains III-V of the CD163 receptor, capable of binding to a region in the SRCR domains III-IV of the CD163 receptor, capable of binding to a region in the SRCR domains III or IV of the CD163 receptor, or a variant thereof.

The domains are in one embodiment arranged as follows with respect to the CD163 sequence:

Domains defined by position of cystein residues corresponds to

- D1: aa 46-146
- D2: aa 154-253
- D3: aa 261-360
- D4: aa 368-467
- D5: aa 473-572

D6: aa 578-677

D7: aa 714-814

D8: aa 819-920

D9: aa 924-1023

5

Numbering according to translated cDNA sequence (Genbank accession no Z22968).

10 Functional equivalents of variants of CD163 will be understood to exhibit amino acid sequences gradually differing from the preferred predetermined sequence, as the number and scope of insertions, deletions and substitutions including conservative substitutions increases. This difference is measured as a reduction in homology and/or identify between the preferred predetermined sequence and the fragment or functional equivalent.

15 All fragments or functional equivalents of CD163 variants are included within the scope of this invention, regardless of the degree of homology that they show to a preferred predetermined sequence of CD163 variants. The reason for this is that some regions of CD163 are most likely readily mutable, or capable of being completely deleted, without any significant effect on the binding activity of the resulting fragment.

20 A functional variant obtained by substitution may well exhibit some form or degree of native CD163 activity, and yet be less homologous, if residues containing functionally similar amino acid side chains are substituted. Functionally similar in this respect refers to dominant characteristics of the side chains such as hydrophobic, basic, neutral or acidic, or the presence or absence of steric bulk. Accordingly, in one embodiment of the invention, the degree of  
25 identity between i) a given CD163 fragment capable of effect and ii) a preferred predetermined fragment, is not a principal measure of the fragment as a variant or functional equivalent of a preferred predetermined CD163 fragment according to the present invention.

30 Fragments sharing at least some homology with a preferred predetermined CD163 fragment of at 50 amino acids, preferably at least 100 amino acids, are to be considered as falling within the scope of the present invention when they are at least about 40 percent homologous with the predetermined CD163 variant or fragment thereof, such as at least about 50 percent homologous, for example at least about 60 percent homologous, such as at least about 70 percent homologous, for example at least about 75 percent homologous, such as  
35 at least about 80 percent homologous, for example at least about 85 percent homologous, such as at least about 90 percent homologous, for example at least 92 percent homologous, such as at least 94 percent homologous, for example at least 95 percent homologous, such as at least 96 percent homologous, for example at least 97 percent homologous, such as at least 98 percent homologous, for example at least 99 percent homologous homologous with

097757-10101  
103107-10101

the predetermined CD163 fragment. In a preferred embodiment the percentages mentioned above also relates to identify percentages.

5 In addition to the variants described herein, sterically similar variants may be formulated to mimic the key portions of the variant structure and that such compounds may also be used in the same manner as the variants of the invention. This may be achieved by techniques of modelling and chemical designing known to those of skill in the art. It will be understood that all such sterically similar constructs fall within the scope of the present invention.

10 In one embodiment the CD163 variant is synthesised by automated synthesis. Any of the commercially available solid-phase techniques may be employed, such as the Merrifield solid phase synthesis method, in which amino acids are sequentially added to a growing amino acid chain. Equipment for automated synthesis of polypeptides is commercially available from suppliers such as Applied Biosystems, Inc. of Foster City, Calif., and may generally be operated according to the manufacturer's instructions. Solid phase synthesis will enable the incorporation of desirable amino acid substitutions into any CD163 variant according to the present invention. It will be understood that substitutions, deletions, insertions or any subcombination thereof may be combined to arrive at a final sequence of a functional equivalent. Insertions shall be understood to include amino-terminal and/or carboxyl-terminal fusions, e.g. with a hydrophobic or immunogenic protein or a carrier such as any polypeptide or scaffold structure capable as serving as a carrier.

20 CD163 variants according to the invention may be synthesised both in vitro and in vivo. Method for in vitro synthesis are well known. When synthesized in vivo, a host cell is transformed with vectors containing DNA encoding the CD163 variant. A vector is defined as a replicable nucleic acid construct. Vectors are used to mediate expression of the CD163 variant. An expression vector is a replicable DNA construct in which a nucleic acid sequence encoding the predetermined CD163 variant, or any functional equivalent thereof that can be expressed in vivo, is operably linked to suitable control sequences capable of effecting the expression of the variant, or equivalent in a suitable host. Such control sequences are well known in the art.

25 Accordingly, one aspect of the invention relates to a DNA sequence encoding a CD163 variant as defined above, the DNA sequence may be a genomic DNA sequence, a cDNA sequence or a mixture of a genomic and a cDNA sequence.

35 Furthermore, the invention relates to a vector comprising the DNA sequence, as well as to a cell comprising said vector, said cell being capable of expressing the DNA sequence, either

0597757-101601